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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,393	08/28/2002	Antonius Helena Adolf Bom	0-1999.475 US	3834

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EXAMINER	
MAIER, LEIGH C	
ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 05/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/049,393	BOM ET AL.	
	Examiner	Art Unit	
	Leigh C. Maier	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-14 and 20-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-14 and 20-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 18, 2005 has been entered.

Status of the Claims

Claims 11 and 12 have been amended. Newly submitted claims 21-30 have been added. Claims 10-20 are pending. Claims 15-19 have been canceled. Claims 11-14 and 20-30 are pending.

Any objection or rejection not expressly repeated has been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. The claims remain subject to the election of species requirement wherein γ–cyclodextrin (broadened by the examiner to α–, β–, and γ–cyclodextrin) was elected as the reversal agent.

Claim Objections

Claims 12, 22, and 27 are objected to because of the following informalities: "Mivacurium" and "(cis) atracurium" are misspelled. Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 11-13 and 20 are again rejected under 35 U.S.C. 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims, as set forth in the previous Office action. Newly added claims 21-23, 25-28, and 30 are included in this rejection.

As noted in previous Office actions, the scope of enablement has two separate components: *Some* cyclodextrins (γ) are enabled for reversing the action of *some* NB agents (those recited in claim 12). The reason that claim 12 is included in the scope rejection is because not *all* cyclodextrins are enabled for this method, even if the independent claim were amended to include the recited agents. Newly added claim 20 is included because γ–cyclodextrin is not enabled for all NB agents that would be embraced by the independent claim.

With regard to the generic limitation "clinically-used neuromuscular blocking agent," this term embraces compounds beyond the scope of those that are specifically recited in the claims. The instant specification provides data demonstrating that γ–cyclodextrins are effective for the recited aminosteroids, and to a lesser extent the recited tetrahydroisoquinoline derivatives. However, there are many other agents that have this utility. See, for example, LEE (Brit. J. Anesth., 2001) at pages 760-761. The mechanism of action by which a cyclodextrin reverses a neuromuscular block is by complexation of the cyclodextrin with the NB agent. The cyclodextrin does not complex with a compound because it happens to be an NB agent. Rather, complexation is based on the chemical structure of the agent. However, an review of the structures of the *known* NB agents shows their variability, not to mention the ones that have yet to be discovered.

Given the variation in the data, it does not seem more likely than not that any given NB agent would necessarily be a good candidate for complexation. As a further testament to this variation of action, ZHANG teaches that a γ–cyclodextrin, not known at the time of the invention, has excellent activity with the aminosteroid derivatives but is completely ineffective for the tetrahydroisoquinoline derivatives and succinylcholine (suxmethonium).

The ZHANG data notwithstanding, the bulk of the existing *in vivo* data suggests that it is more likely than not that γ–cyclodextrins are enabled for the recited NB agents. See also TARVER et al (Bioorg. Med. Chem., 2002) and ADAM et al (J. Med. Chem., 2002). A review of this data as well as that in the instant specification appears to support the fact the rocuronium is a special case and is more likely than not also reversed by a β–cyclodextrin. Applicant contends that the specification presents a representative amount of NB agents that work within the scope of the present claims. The examiner agrees to the extent that as stated above, the data indicate that it is more likely than not that any particular γ–cyclodextrin would be expected to work in this method. However, there is a distinct lack of data for β–cyclodextrins. As is well known in the art and demonstrated in Applicant's post-filing publications, the data for γ–cyclodextrins cannot be extrapolated to β–cyclodextrins.

In light of the forgoing, it is concluded that one of ordinary skill would require undue experimentation at great expense in order to practice the invention. In reviewing the data in post-filing publications, it is noted that the *in vitro* data is not necessarily predictive of *in vivo* results. Therefore, one of ordinary skill would be unable to rely on *in vitro* results as a screening method, thereby adding expense to the practice of the invention.

Double Patenting

Claims 11-14 are again rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 9 of U.S. Patent No. 6,670,340, as set forth in the previous Office action. New claims 21-30 are also included in this rejection.

Applicant has indicated a willingness to submit a terminal disclaimer, if necessary, upon indication of allowability.

Allowable Subject Matter

Claims 14 and 29 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

See discussion of DÉSIRÉ in the previous Office action. The reference does not teach or fairly suggest the instant method wherein the NB agents are those recited in claim 12. All claims appear to be free of the art but are subject to other rejections set forth above. A claim limited to the recited NBs and γ–CD would appear to be fully enabled and free of the art. As per discussion above, a claim to rocuronium and β–CDs would be fully enabled and free of the art.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Tuesday, Thursday, and Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson (571) 272-0661, may be contacted. The fax number for Group 1600, Art Unit 1623 is (703) 872-9306.

Visit the U.S. PTO's site on the World Wide Web at http://**www.uspto.gov**. This site contains lots of valuable information including the latest PTO fees, downloadable forms, basic search capabilities and much more.

Leigh C. Maier

Leigh C. Maier
Primary Examiner
May 6, 2005